## AMENDMENTS TO THE CLAIMS

Please amend Claims 85, 90, 107 and 109-111 as shown below:

1-84. **(Cancelled)**

85. **(Currently amended)** A method for assessing the binding affinity between a candidate peptide and a target protein, said method comprising:

obtaining a collection of sequence and binding strength data for at least one peptide of known affinity for said target protein;

obtaining sequence data for said candidate peptide;

determining a first affinity for the candidate peptide for said target protein using a first predictive method, wherein said first predictive method employs ~~determination is based, in part, upon~~ the candidate peptide sequence data;

determining a second affinity for the candidate peptide for said target protein using a second predictive method, wherein said second predictive method employs ~~determination is based, in part, upon~~ the candidate peptide sequence data, said second predictive method further comprising ~~the use of said collection of sequence and binding strength data~~ comparing the candidate peptide sequence data to the sequence data of the peptide of known affinity, and wherein said second predictive method is different from the first predictive method;

scaling said first affinity;

scaling said second affinity, said scaling of the first and second affinities comprising a method selected from the group consisting of 1) linearly scaling each affinity so that it has a value between 1 and 0, 2) nonlinearly scaling each affinity so that it has a value between 1 and 0, and 3) scaling the affinity in a manner so a particular type of method can have a different weight, wherein a value is maintained between 1 and 0;

combining said first and second affinities ~~wherein the first and second affinities are scaled before they are combined, said scaling comprising a method selected from the group consisting of 1) linearly scaling each affinity so that it has a value between 1 and 0, 2) nonlinearly scaling each affinity so that it has a value between 1 and 0, and 3) scaling~~

~~the affinity in a manner so a particular type of method can have a different weight, wherein a value is maintained between 1 and 0~~; and

evaluating the combined first and second affinities as a basis for assessing the binding affinity between the candidate peptide and the target protein.

86. **(Previously presented)** The method of Claim 85, wherein said target protein is a MHC class I protein and wherein said peptide comprises an epitope whereby said MHC class I protein binds to said peptide.

87. **(Currently amended)** The method of Claim 85, wherein ~~the first and second affinities are scaled before they are combined,~~ said scaling ~~comprising~~ comprises linearly scaling each affinity so that it has a value between 1 and 0.

88. **(Previously presented)** The method of Claim 85, wherein the candidate peptide is generated by dividing the sequence data of a known protein into ninemer or tenmer fragments.

89. **(Previously presented)** The method of Claim 85, wherein said first predictive method and said second predictive method are selected from the group consisting of quadratic programming, linear programming, anchor scoring, and profile-based scoring.

90. **(Currently amended)** A method for evaluating the affinity of a candidate peptide for a target protein, said method comprising:

obtaining for a plurality of known peptides, a collection of sequence and binding affinity information for said target protein;

obtaining sequence data for the candidate peptide;

predicting a first affinity for said candidate peptide for said target protein ~~based, in part, upon~~ by evaluating ~~the evaluation of~~ the collection of sequence and binding affinity information for the plurality of known peptides, wherein the evaluation of the collection of sequence information comprises a comparison of the peptide sequences of the plurality of known peptides to the sequence data for the candidate peptide;

predicting a second affinity for said candidate peptide for said target protein by ~~based, in part, upon the evaluation of~~ evaluating the collection of sequence and binding affinity information for the plurality of known peptides in a manner that differs from the first affinity prediction;

normalizing said first affinity to generate a first vote;

normalizing said second affinity to generate a second vote; and

combining the first and second votes to obtain a score, wherein the score reflects the overall affinity of said candidate peptide for said target protein.

91. **(Previously presented)** The method of Claim 90, wherein said protein is a MHC class I protein and wherein said peptide comprises an epitope whereby the MHC class I protein binds to the peptide.

92. **(Previously presented)** The method of Claim 90, wherein said first and second affinity predictions are predicted by a method selected from the group comprising quadratic programming, linear programming, anchor scoring, and profile-based scoring, and wherein the second method is not the same method selected for the first method.

93. **(Withdrawn)** A method of predicting the binding strength of a candidate peptide for a target protein, said method comprising:

obtaining sequence data for a candidate peptide;

obtaining sequence and binding strength data for at least one peptide of known affinity for a target protein;

generating a first vote by scaling a first affinity prediction of the candidate peptide for said target protein;

generating a second vote by scaling a second affinity prediction of the candidate peptide for said target protein, wherein at least one of said first and said second predictions uses the sequence and binding strength data for the at least one peptide of known affinity for said target protein; and

combining the first and second votes to create a score, wherein said score reflects the relative binding strength of the candidate peptide for said target protein.

94. **(Withdrawn)** The method of Claim 93 further comprising:

ordering the candidate peptide so as to create a list according to the candidate peptide's score, wherein a candidate peptide with a largest score is first in said list and a candidate peptide with a lowest score is last in said list;

separating said list into a R1, a R2, and a R3 rankings, wherein said R1 ranking is defined as a point in the list where a number of moderate binding strength peptides is greater than a number of high binding strength peptides, wherein said R2 ranking is

defined as a point in the list where a number of low binding strength peptides is greater than the sum of a number of moderate and high binding strength peptides, and wherein said R3 ranking is defined as a point in the list for a last low binding strength peptide;

assigning a binding level class of high, moderate, low, or none to each candidate peptide on the list based on if it is above R1, between R1 and R2, between R2 and R3, and below R4 respectively; and

selecting a candidate peptide from the list based on the assigned binding level class associated with the candidate peptide, thereby selecting a peptide with a desired level of affinity for a target protein.

95. **(Withdrawn)** The method of Claim 94, wherein said target protein is a MHC class I protein and wherein said peptide comprises an epitope whereby said MHC class I protein binds to said peptide.

96. **(Withdrawn)** The method of Claim 94, wherein generating the vote from the affinity predictions comprises a method selected from the group consisting of 1) linearly scaling each affinity prediction so that the vote has a value between 1 and 0, 2) nonlinearly scaling each affinity prediction so that the vote has a value between 1 and 0, and 3) scaling each affinity prediction in a manner so a particular type of method can have a different weight in voting, wherein the value is maintained between 1 and 0.

97. **(Withdrawn)** The method of Claim 94, wherein said first and second affinity predictions are predicted by a method selected from the group comprising quadratic programming, linear programming, anchor scoring, and profile-based scoring, and wherein the second method is not the same method selected for the first method.

98. **(Withdrawn)** The method of Claim 94, wherein the high binding strength peptide is defined as one with an $IC_{50}$ of less than 1nM, wherein the moderate binding strength peptide is defined as one with an $IC_{50}$ of more than 1nM and less than 100nM, wherein the low binding strength peptide is defined as one with an $IC_{50}$ of more than 100nM and less than 10 μM, and wherein no binding is defined as an $IC_{50}$ of more than 10 μM.

99. **(Withdrawn)** The method of Claim 94, wherein the method is repeated for a second candidate peptide, thereby generating a second score for the second candidate peptide, wherein said score is used to order the second candidate in the list.

100. **(Withdrawn)** The method of Claim 94, wherein the binding strength data for at least one peptide of known affinity for a target protein is selected from the group comprising a dissociation constant, $k_a$, $k_d$, or $IC_{50}$.

101. **(Withdrawn)** The method of Claim 97, wherein said profile-based scoring uses a clustering heuristic selected from the group comprising iterative multiple alignment, letter frequencies, and position dependencies reflected by two (2) tests.

102. **(Withdrawn)** The method of Claim 101, wherein said profile-based scoring employs a principle selected from the group comprising dimensionality reduction, multiple intra-allelic motifs, and anchor selection.

103. **(Withdrawn)** A method for generating an epitope useful in the treatment of cancer, said method comprising:

obtaining sequence and binding strength data for at least one epitope of known affinity for a MHC class I protein;

obtaining sequence data for a candidate epitope for a MHC class I protein;

predicting a first affinity for the candidate epitope with said target MHC class I protein using a first method;

predicting a second affinity for the candidate epitope with said target MHC class I protein using a second method, wherein at least one of said first and said second methods uses the data for the epitope of known affinity;

attributing a vote to each of said first and second affinities;

combining the two votes to obtain a vote total for the candidate epitope;

ordering the candidate epitope in a list according to the candidate epitope's vote total, wherein a candidate epitope with a highest vote total is first in said list and a candidate epitope with a lowest vote total is last in said list;

separating said list into a R1, a R2, and a R3 ranking, wherein said R1 ranking is defined as a point in the list where a number of moderate binding strength peptides is greater than a number of high binding strength peptides, wherein said R2 ranking is defined as a point in the list where a number of low binding strength peptides is greater than the sum of a number of moderate and high binding strength peptides, and wherein said R3 ranking is defined as a point in the list for a last low binding strength peptide, and

wherein the high binding strength peptide is defined as one with an $IC_{50}$ of less than 1nM, wherein the moderate binding strength peptide is defined as one with an $IC_{50}$ of more than 1nM and less than 100nM, wherein the low binding strength peptide is defined as one with an $IC_{50}$ of more than 100nM and less than 10 μM, and wherein no binding is defined as an $IC_{50}$ of more than 10 μM;

assigning a binding level class of high, moderate, low, or none to each candidate epitope in the list based on if it is above R1, between R1 and R2, between R2 and R3, and below R4 respectively;

selecting the candidate epitope from the list based on the assigned binding level class associated with the candidate epitope, wherein said assigned binding level class is either in the moderate or lower levels of the binding classes; and

producing or isolating a protein that comprises said epitope, thereby generating an epitope that is useful in the treatment of cancer.

104. **(Withdrawn)** An iterative multiple alignment (*aln*) method of predicting the relative binding affinity of a peptide for a MHC protein, comprising:

obtaining sequence and affinity information for a set of known epitopes for a MHC protein;

deriving a motif from said information for a set of known epitopes via an iterative multiple alignment heuristic, wherein said iterative multiple alignment heuristic builds a profile by adding a new sequence to an existing cluster until a stop condition is encountered;

generating a score for said peptide based on its similarity to said motif, wherein the iterative multiple alignment heuristic is also used on said peptide; and

predicting the relative binding affinity of said peptide for said MHC protein based on said score.

105. **(Withdrawn)** A letter frequency (LetFq) method of predicting the relative binding affinity of a peptide for a MHC protein, comprising:

obtaining sequence and affinity information for a set of known epitopes for said MHC protein;

deriving a motif from said information for a set of known epitopes via a letter frequency heuristic, wherein said letter frequency heuristic recursively splits a sequence cluster into two disjoint subclusters, wherein said splitting is according to a sequence letter at a chosen profile position, and wherein said letter frequency heuristic repeats the previous procedure for the two subclusters thus formed;

generating a score for said peptide based on its similarity to said motif; and

predicting the relative binding affinity of said peptide for said MHC protein based on said score.

106. **(Withdrawn)** A method based on $\chi^2$ statistical significance ($Ki^2$) tests for predicting the relative binding affinity of a peptide for a MHC protein, comprising:

obtaining sequence and affinity information for a set of known epitopes for said MHC protein;

deriving a motif from said information for a set of known epitopes according to dependencies between peptide positions, revealed by a $Ki^2$ significance test, wherein said $Ki^2$ significance test recursively splits a sequence cluster into two disjoint subclusters, wherein said splitting is according to a sequence letter at a chosen profile position, and wherein said $Ki^2$ significance test repeats the previous procedure for the two subclusters thus formed;

generating a score for said peptide based on its similarity to said motif; and

predicting the relative binding affinity of said peptide for said MHC protein based on said score.

107. **(Currently amended)** A method for assessing the binding affinity between a candidate epitope and a MHC protein, said method comprising:

obtaining a collection of sequence and binding strength data for at least one epitope of known affinity for said MHC protein;

obtaining sequence data for said candidate epitope;

predicting a first binding affinity for the candidate epitope for said MHC protein using a first predictive method, wherein said prediction is a function of ~~based, in part, upon~~ the candidate epitope sequence data;

predicting a second binding affinity for the candidate epitope for said MHC protein by using a second predictive method, wherein said prediction comprises~~is based, in part, upon~~ a comparison between the sequence data for the at least one epitope of known affinity and the sequence data for the candidate epitope in order to determine a similarity, and then using the similarity between the two sequences to predict the second binding affinity based upon the affinity of the peptide of known affinity~~the candidate peptide sequence data, said second predictive method further comprising the use of the collection of sequence and binding strength data for the at least one epitope of known affinity for said MHC protein~~, and wherein said second predictive method is different from said first predictive method;

scaling the first and second predicted binding affinities before they are combined, said scaling comprising a method selected from the group consisting of 1) linearly scaling each affinity so that it has a value between 1 and 0, 2) nonlinearly scaling each affinity so that it has a value between 1 and 0, and 3) scaling the affinity in a manner so a particular type of method can have a different weight, wherein a value is maintained between 1 and 0;

combining said first and second binding affinities ~~wherein the first and second binding affinities are scaled before they are combined, said scaling comprising a method selected from the group consisting of 1) linearly scaling each affinity so that it has a value between 1 and 0, 2) nonlinearly scaling each affinity so that it has a value between 1 and 0, and 3) scaling the affinity in a manner so a particular type of method can have a different weight, wherein a value is maintained between 1 and 0~~; and

evaluating the combined first and second binding affinities as a basis for assessing the binding affinity between the candidate epitope and the MHC protein.

108. **(Previously presented)** The method of Claim 107, wherein the MHC protein is a MHC class I protein.

109. **(Currently amended)** A method for assessing the binding affinity between a candidate peptide and a target protein, said method comprising:

obtaining a collection of sequence and binding strength data for at least one peptide of known affinity for said target protein;

obtaining sequence data for said candidate peptide;

determining a first affinity for the candidate peptide for said target protein using a first predictive method, wherein said determination employs ~~is based, in part, upon~~ the candidate peptide sequence data to determine the first affinity;

determining a second affinity for the candidate peptide for said target protein using a second predictive method, wherein said determination employs ~~is based, in part, upon~~ the candidate peptide sequence data to determine the second affinity, said second predictive method further comprising comparing the candidate peptide sequence data to the sequence data of the peptide of known affinity, ~~the use of said collection of sequence and binding strength data,~~ and wherein said second predictive method is different from the first predictive method;

scaling the first and second affinities, said scaling comprising linearly scaling each affinity so that it has a value between 1 and 0;

combining said first and second affinities wherein the first and second affinities are scaled before they are combined~~, said scaling comprising linearly scaling each affinity so that it has a value between 1 and 0~~; and

evaluating the combined first and second affinities as a basis for assessing the binding affinity between the candidate peptide and the target protein.

110. **(Currently amended)** A method for assessing the binding affinity between a candidate peptide and a target protein, said method comprising:

obtaining a collection of sequence and binding strength data for at least one peptide of known affinity for said target protein;

obtaining sequence data for said candidate peptide;

determining a first affinity for the candidate peptide for said target protein using a first predictive method, wherein said first predictive method employs ~~determination is based, in part, upon~~ the candidate peptide sequence data to determine the first affinity;

determining a second affinity for the candidate peptide for said target protein using a second predictive method, wherein said second predictive method employs ~~determination is based, in part, upon~~ the candidate peptide sequence data to determine the second affinity, said second predictive method further comprises comparing the candidate

peptide sequence data to the sequence data of the peptide of known affinity~~comprising the use of said collection of sequence and binding strength data~~, and wherein said second predictive method is different from the first predictive method;

scaling the first and second affinities, said scaling comprising nonlinearly scaling each affinity so that it has a value between 1 and 0;

combining said first and second affinities, wherein the first and second affinities are scaled before they are combined~~, said scaling comprising nonlinearly scaling each affinity so that it has a value between 1 and 0~~; and

evaluating the combined first and second affinities as a basis for assessing the binding affinity between the candidate peptide and the target protein.

111. **(Currently amended)** A method for assessing the binding affinity between a candidate peptide and a target protein, said method comprising:

obtaining a collection of amino acid sequences ~~sequence~~ and binding strength data for at least one peptide of known affinity for said target protein;

obtaining a sequence ~~data~~ for said candidate peptide;

determining a first affinity for the candidate peptide for said target protein using a first predictive method, wherein said determination ~~is~~ employs ~~based, in part, upon~~ the candidate peptide sequence ~~data~~ in order to determine the first affinity;

determining a second affinity for the candidate peptide for said target protein using a second predictive method, wherein said determination ~~is~~ employs ~~based, in part, upon~~ the candidate peptide sequence ~~data~~ in order to determine the second affinity, said second predictive method further comprises comparing the candidate peptide sequence to the sequence of the peptide of known affinity~~comprising the use of said collection of sequence and binding strength data~~, and wherein said second predictive method is different from the first predictive method;

scaling the first and second affinities in a manner so a particular type of predictive method can have a different weight, wherein a value is maintained between 1 and 0;

combining said first and second affinities wherein the first and second affinities are scaled before they are combined~~, said scaling comprising scaling the affinity in a~~

~~manner so a particular type of method can have a different weight, wherein a value is maintained between 1 and 0~~; and

evaluating the combined first and second affinities as a basis for assessing the binding affinity between the candidate peptide and the target protein.

## SUMMARY OF INTERVIEW

Exhibits and/or Demonstrations

None

Identification of Claims Discussed

The claims were generally discussed.

Identification of Prior Art Discussed

Rognan et al. was discussed.

Proposed Amendments

Amendments similar to those presented herein were discussed.

Principal Arguments and Other Matters

Applicant's representative noted that the previous amendment only incorporated elements from dependent claims into the independent claims and did not raise any new issues and questioned whether the finality of the Office Action is appropriate. Applicant's representative also noted that the claimed method was directed towards combining the results of two predictive methods to obtain a different prediction of affinity rather than combining various subparts to obtain a single prediction based on a single technique. It was also noted that the scaling and combining steps in the pending claims are not taught, in relation to predicted affinities, in the cited art.

Results of Interview

Applicants agreed to submit an amendment to further clarify the claims. The Examiners generally agreed that the presently submitted amendments should resolve the §112 rejection and further distinguish the claimed method from the cited art.